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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/729,644	11/30/2000	Glenn Pierce	760100.450	3051

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/729,644	PIERCE ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 February 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *26 February 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1-71 and 98-104*.

Claim(s) withdrawn from consideration: _____.

8.☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Continuation of 2. NOTE: Claim 1 had been amended to recite "the biocompatible substance is selected from the group consisting of: a polysaccharide, a PVA sponge, and a lactic acid/glycolic acid polymer". Although "polysaccharides" were previously set forth in claim 51 and a copolymer comprising lactic acid and glycolic acid was set forth in claim 63, claims 51 and 63 were limited to a biological matrix comprising a polysaccharide or copolymer comprising lactic acid and glycolic acid. In contrast, claim 1 is merely directed to a "biocompatible substance" comprising a polysaccharide or a lactic acid/glycolic acid polymer. Thus, the scope of claim 1 is different from the scope of the claims previously considered. Likewise, the PVA sponge of claim 1 is not found in the previously examined claims. As the proposed amendments to claim 1 include addition of subject matter that has not been previously considered, additional search and examination would be required to determine patentability of the claim and all claims depending therefrom. In addition, amended claims 2 and 103, and new claim 105 recite a stimulating agent that is "a mutated FGF". The new limitation is clearly broader in scope than the "mutated FGF-2" previously considered as a limitation of claim 10 and therefore would require additional search and examination..

Continuation of 5. does NOT place the application in condition for allowance because:

CLAIM REJECTIONS UNDER 35 USC 112, FIRST PARAGRAPH

In response to the prima facie case and arguments of record, Applicant cites In re Wands and Atlas Powder Co. v. E.I. DuPont De Nemours & Co. and, while apparently acknowledging that experimentation would be required to practice the full scope of the invention, argues that the amount of experimentation is not undue according to the legal standard. Applicant submits that the production of the claimed device and methods of using the device for systemic delivery of a bioactive agent would require only routine screening because the specification clearly demonstrates effective cellular infiltration and gene expression using the claimed device. Applicant urges that the skilled artisan could readily prepare devices comprising nucleic acid constructs expressing a bioactive agent, implant these into a subject, and establish that the bioactive agent was expressed and systemically available at sufficient levels.

These arguments have been fully considered but are not deemed persuasive. With regard to the legal standard for "undue experimentation", In re Wands is clear, "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman ...They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims" (8 USPQ2d 1400, page 1404). The present arguments appear to be Applicant's opinion of what is routine experimentation and not the legal analysis set forth in In re Wands. In contrast, analysis of the instant claims according to the "Wands factors" is clearly set forth in the Office Action mailed 6 December 2002, and the arguments and evidence provided by Applicant to rebut the prima facie case has been found unpersuasive for the reasons set forth in the Office Action mailed 26 August 2003. Applicant's arguments regarding the routine nature of "optimizing" the claimed invention is addressed in the paragraph bridging pages 11-12 of the 26 August Office Action.

With regard to enablement for the full scope of the many embodiments encompassed by the claims, Applicant submits that there is no requirement that every embodiment be shown to be fully operative. Applicant cites Atlas Powder Co. v. E.I. DuPont de Nemours & Co. as stating, "[it is] not a function of the claims to specifically exclude possible inoperative substances" and urges the existence of one or more inoperative species encompassed within the genus does not render claims to the genus non-enabled. However, it must be pointed out that the sentence immediately following the statement cited by Applicant reads, "[o]f course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid" (224 USPQ 409, page 414). In the instant case, none of the dozens of embodiments set forth in the claims could be used for the purpose asserted in the specification with out substantial empirical experimentation. Clearly, therefore, the number of inoperative combinations is significant and would force one of ordinary skill in the art to experiment unduly.

Applicant takes issue with the Examiner's contention that expression levels sufficient for systemic delivery of a bioactive agent would necessarily be of much greater magnitude and duration than those required for localized expression, as described in Roth et al. However, it appears that Applicant has misconstrued the Examiner's position. The remarks were directed specifically to treatment of non-small cell lung cancers using p53 as a bioactive agent as taught by Roth et al. Applicant had cited Roth et al. as evidence of enablement forth the instant claims. The Examiner's contention is merely that the teachings of Roth et al., which are limited to treating non-small cell lung cancers by direct injection of a retroviral vector expressing a wild-type p53 gene, are not enabling for the instant claims because the claims are explicitly limited to systemic delivery of the bioactive agent. It is highly unpredictable whether one could effectively treat non-small cell lung cancer by systemic administration of p53. Furthermore, as the teachings of Roth et al. are specifically directed to treating non-small cell lung cancers by direct injection of a retroviral vector expressing a wild-type p53 gene it is unclear how these teachings could be enabling for the broad scope of the instant claims.

Next, Applicant cites In re Brana and argues that enablement of the claimed invention does not require a demonstration that the invention may be used therapeutically because the Court held that the FDA's requirements of testing for safety and effectiveness are not required by the patent laws. Applicant's point that the FDA's requirements need not be met for patentability is taken. However, the Brana court, citing In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961), states, "proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility" (page 1442). The claims at issue in In re Brana were directed to a specific chemical compound having established antitumor activity, which was demonstrated in a recognized experimental animal model. In contrast, the instant claims are directed to an in situ bioreactor comprising active ingredients having broadly divergent properties, and the disclosure provides no evidence that the claimed invention can be used as asserted in the specification despite the established unpredictability of the art. Clearly, the courts finding in In re Brana does not support enablement for the instant claims.

Applicant's arguments have been fully considered but are not deemed persuasive individually or as a whole. Therefore the claims stand rejected as lacking enablement under 35 U.S.C. §112, first paragraph.

Continuation Sheet (PTO-303) **Application No.**

CLAIM REJECTIONS UNDER 35 USC 102

Applicant's remarks with regard to patentability of the finally rejected claims over the art of record merely reiterate arguments that were fully addressed in the Final Office Action (see pages 12-14 of the 26 August Office Action). As the present amendment has not been entered, Applicant's arguments as to patentability of the claims as amended after final rejection are moot..